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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,655	12/05/2003	Istvan Szelenyi	081117-0126	8949

41552 7590 01/07/2010

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
01/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SIP_Docket@mwe.com

Office Action Summary	Application No.	Applicant(s)	
	10/727,655	SZELENYI ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-28* is/are pending in the application.

4a) Of the above claim(s) *16-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15 and 23-28* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

2. Acknowledgement is made of applicant's filing of amendment/remarks on 11/05/2009. By the amendment, claims 12-14, 24 and 25 have been amended and claim 23 has been cancelled. Claims 12-15 and 23-28 are currently pending for prosecution on the merits.

3. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12-15 and 23-28 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for treating neuralgia pain or neuropathic pain with a combination of retigabine and the specific voltage gated sodium channel inhibitor such as tolperisone, does not reasonably provide enablement for the treatment of said condition with a combination of retigabine with "a voltage gated sodium channel inhibitor or a therapeutically utilizable salt thereof" or "riluzole, propafenone,…" and/or "eperisone, silperisone and tolperisone analogs…". The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Applicant's argument in Response filed on 11/05/2009 asserts that "One skilled in the art, aware of the teachings of Galer et al. would not come to the conclusion that 1) any sodium blocker would be effective to treat neuropathic pain or 2) that any sodium channel blocker would be expected to have an added benefit when used in conjunction with retigabine. ..because riluzole has been found to be ineffective for this purpose" (page 5, last paragraph to bridge paragraph in page 6). Furthermore, applicant asserts that "two drugs indicated for treatment of neuropathic pain renders obvious their combination…is not obvious because of the complexity of cellular mechanisms, such as the sodium-potassium ATPase pum…The interplay and distribution of such pumps, in conjuction with voltage-gated sodium and potassium channels translates to a level of unpredictability a to whether each drug would have the same impact...Thus, one skilled in the art is not instilled with a reasonable expectation of success that the drug combination would have synergistic or even simple additive beneficial effects" (page 6,

paragraph 3); and "one skilled in the art would not expect lidocaine and tolperisone to necessarily behave in a similar manner because while there are some similarities, there are also differences" (page 7, last paragraph).

Given the breadth, the disparate nature of compounds that is presently claimed, the highly unpredictable state of the art where many specific differences or different physicochemical properties are existed among unrelated structural compounds or even structurally related compounds and the limited number of exemplified "voltage-gated sodium channel inhibitor", especially in light of the applicant's Remarks, the examiner determines that one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to make/use the claimed combination of retigabine and a voltage gated sodium channel inhibitor including riluzole, propafenone, lidocaine, flecainide, metixen, eperisone, silperisone and tolperisone analogs that would be enabled in this specification (The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976))).

The examiner acknowledges that the Office does not require the present of (all) working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art as acknowledged by the applicant and furthermore, given

that the applicant does not provide sufficient guidance or direction as to how to make and use the full scope of the presently claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of the elected species for the full scope of the presently claimed subject matter. Absent such evidence or reasoning, applicant has failed to obviate the rejection of the instant claims under 35 USC 112, first paragraph (for the lack of scope of enablement).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 14-15 and 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "tolperisone analog". The scope of term "tolperisone" encompasses "eperisone and silperisone". Applicant's redundancy or repetition of term "tolperisone analog" leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 12-13 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rundfeldt et al. (US 6117900) in view of Cai et al. (US 6281211), and further in view of the applicant's admitted prior art of the record (page 1, line 25 through page 4, line 3).

Rundfeldt teaches the use of retigabine for the treatment of neuropathic pain in an animal, wherein said compound is administered in various dosage forms including oral or parenteral forms (abstract; column 8, lines 26-37; claims).

Cai teaches the use of Na+ channel blocker such as riluzole, lidocaine, propafenone and semicarbazone derivatives for the treatment neuropathic pain in mammals including humans (see particularly "Related Background Art" in column 1, lines 18-56 and "Summary of Actions"; abstract).

Applicant's admitted prior art of records teaches the use of sodium channel inhibitor or tolperisone in normalizing or maintaining muscle tone (spasticity).

The teaching of Rundfeldt differs from the claimed invention in the combination use of retigabine and sodium channel blocker such as lidocaine, propagenone and riluzole. To incorporate such teaching into the teaching of Rundfeldt, would have been obvious in view of Cai who teaches the use of sodium channel blocker such as riluzol, lidocaine and propagenone for the treatment of neuropathic pain.

Above references in combination make clear that retigabine and sodium channel blocker such as lidocaine, propageneone and riluzole have been individually used for the treatment of neuropathic pain. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).

With respect to the determination of various dosage forms (e.g., orally, rectally, intravenously, transdermally, subcutaneously or intracutaneously) and the current administration regimen of two drugs (e.g., simultaneously, separately or consecutively), such determination of appropriate dosage forms and administration regiment for treatment involving each of the above

mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of drug delivery information provided in the prior art references.

With respect to "said neuralgia pain or neuropathic pain is accompanied by an increase in muscle tone" in claims 26 and 27, the prior art reference(s) does/do not specifically mention the feature of the presence of "an increase in muscle tone" in the prior method. However, one having ordinary skill in the art would have expected at the time of the invention was made that such feature of the instant invention would have been characteristic of the modified prior art method. Especially, considering the state of art knowledge at the time of the invention was made as evidenced by the applicant's admission, one having ordinary skill in the would have expected that the administration of the instant combination containing sodium channel inhibitor would benefit the patient suffering from neuropathic pain accompanying with the increase in muscle tone (spasticity). Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to "human" application of the instant combination, a person having ordinary skill in the art has basis for perceiving those in vivo studies in the cited references as constituting recognized screening procedures with clear relevance to utility in humans.

Response to Arguments

7. Applicant's arguments filed 11/05/2009 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, again, the prior art references in combination (Rundfelt and Cai) make clear that retigabine and sodium channel blocker such as lidocaine, propageneone and riluzole have been individually used for the treatment of neuropathic pain. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980). Thus, in absence of superior or unexpected results of the combination (generally by showing data or result that the claimed combination achieves unexpected or superior results), the examiner maintains the rejection of the record.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614